UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
OFFICE OF PESTICIDE PROGRAMS REGISTRATION DIVISION (7505P)

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CONTAINS CONFIDENTIAL BUSINESS INFORMATION

DP Barcode No.: D435645 File Symbol No.: 432-RLII Decision No.: 520689
PC Code: 129140 Company Name: Bayer Environmental Science
Food Use: No Action Code: R 060 Product Name: Bayothrin Technical

Date: February 15, 2018

SUBJECT: Product Chemistry Review of the Proposed Manufacturing Use Product, Bayothrin Technical

FROM: Bruce F. Kitchens, Chemist
Chemistry, Inert and Toxicology Assessment Branch/RD (7505P)
Registration Division (7505P)

Bruce F. Kitchens
SBM

TO: RM #03, Kable Davis/Timothy Ciarlo
Invertebrate and Vertebrate Branch I
Registration Division (7505P)

INTRODUCTION:

The registrant, Bayer Environmental Science, is submitting an application for the registration of the new manufacturing use product, Bayothrin Technical. The active ingredient in this product is Transfluthrin at a label nominal concentration of 99.68% a.i. This product is intended for use in the manufacture of insecticide end-use products. In support of this request, the registrant has submitted a basic Confidential Statement of Formula (CSF) dated 11 July 2016, a draft label, and product chemistry data contained in MRID#s 496178-02 thru 496178-22. The Chemistry, Inerts and Toxicology Assessment Branch (CITAB) has been asked to review this submission.

SUMMARY OF FINDINGS:

CITAB has reviewed this submission and reports the following findings:

1. This product is produced from an integrated formulation system. This means that the product is the result of intended chemical reactions.

2. All impurities have been assayed and identified by the registrant. The registrant has not declared any impurities of toxicological concern in this product. All impurities have a nominal concentration and upper certified limits.

3. The nominal concentration of the active ingredient listed on the proposed CSF and the draft label are the same.

4. The draft label contains the appropriate storage and disposal statements.

5. The active ingredient's certified limits as proposed on the basic CSF are acceptable.

CONCLUSIONS:

CITAB has reviewed this submission and concludes the following:

1. The basic formula CSF for the proposed manufacturing use product, Bayothrin Technical dated 11 July 2016 is acceptable.

2. This submission satisfies the data requirements as specified in 40 CFR 158.320, 158.325, 158.330, 158.340, 158.345, 158.350, and 158.355 with respect to product identity and composition, description of materials used to produce the product, description of production process, discussion of formation of impurities, preliminary analysis, certified limits, and enforcement analytical method.

3. This submission satisfies the data requirements as specified in 40 CFR 158.310 with respect to physical and chemical properties 830.6314 Oxidation/reduction:chemical incompatibility. The reducing properties were evaluated. This data is required.

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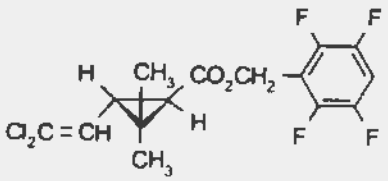
830.1550. Product Identity & Composition: (MRID No. 496478-02)

Common Name:	Transfluthrin
Chemical Name (CAS):	cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, (2,3,5,6-tetrafluorophenyl)methyl ester, (1R, 3S)-
(IUPAC):	2,3,5,6-tetrafluorobenzyl(1R, 3S)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate
CAS No.:	118712-89-3
PC Code No.:	129140
Empirical formula:	$C_{15}H_{12}Cl_2F_4O$
Molecular Weight:	371.2 g/mol
Structural formula:	



TRANSFLUTHRIN

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Table 1. Manufacturing and Impurity Data for Bayothrin Technical

/GLN	Requirement	MRID	Status	Details and /or Deficiency
830.1550	Product Identity and Composition	496178-02	A	The nominal concentration of the active ingredient (98.68%) is supported by 5 batch analysis & agrees with the label claim nominal concentration. [redacted] impurities are listed on the CSF.
8301600	Description of Materials Used to Produce the Product	496178-03	A	The product specification sheets (MSDS) for all the starting materials have been provided by the registrant
830.1620	Description of Production Process	496178-03	A	The active ingredient is produced in a two-step batch integrated process. The production process has been described in full detail. The reaction conditions, amounts of chemicals in each step, duration of time, and the yields in each step have been provided. The QA steps involved in each step have been described.
830.1670	Discussion of Formation of Impurities	496178-04	A	The registrant has provided the complete mechanisms of formation, quantification and identification of all the impurities present at the levels of ≥ 0.1%. Total of [redacted] impurities have been listed on the CSF. No toxic impurity was reported during the synthesis.
830.1700	Preliminary Analysis	496178-05	A	The registrant has provided 5 batch analysis for the TGAI. The AI & impurities were identified and quantified by using chiral-HPLC/UV and an external standard method. The five batch analysis supported the CSF for basic formulation.
830.1750	Certified Limits	see basic csf 7/11/16	A	The proposed certified limits for the AI & for the impurities are based on the five batch analytical results.
830.1800	Enforcement Analytical Method	496178-06 496178-07	A	A chiral HPLC/UV method was used for the determination of the active ingredient and impurity content in the TGAI/MUP using an external standard.

A = Acceptable; N = unacceptable (see Deficiency); N/A = Not Applicable; G = Data gap; I = In progress or need upgrade; U = Up-grade (additional information required

830 Series Subgroup B (Physical-Chemical Properties)

Table 2: Physical and Chemical Properties of Bayothrin Technical

GLN	Requirement	MRID	Status	Result or Deficiency
830.6302	Color	496178-08	Y	Off-white
830.6303	Physical state	496178-08	Y	Solid
830.6304	Odor	496178-08	Y	Toluene like odor
830.6313	Stability to normal and elevated temperatures, metals, and metal ions	496178-09 496178-13	Y	The test substance was stable after storage for 42 months at 25°C/60% r.h. Waiver granted due to expected lack of exposure to elevated temperature during production or storage. The test substance is no expected to contact metals. This portion of the data requirement is waived.
830.6314	Oxidation/reduction: chemical incompatibility	496178-10	U	Product has oxidizing properties when subjected to burning with a burn rate of 1.4 mm/s. A reference mixture of barium nitrate had a burn rate of 1.3 mm/s. Reduction properties were not evaluated.
830.6315	Flammability	496178-11	Y	119°C
830.6316	Explodability	496178-12	Y	Test substance is not sensitive to mechanical shock, mechanical friction. The test substance is not thermally sensitive.
830.6317	Storage stability	496178-13	Y	The test substance was stable after storage for 42 months at 25°C/60% r.h.
830.6319	Miscibility		N/A	Not required
830.6320	Corrosion characteristics	496178-13	Y	Test substance remained a yellow beige solid over the course of the study.
830.7000	pH	496178-15	Y	5.73
830.7050	UV/Visible absorption	496178-07	Y	UV spectrum provided
830.7100	Viscosity		N/A	Test substance is a solid.
830.7200	Melting point	496178-17	Y	32°C
830.7220	Boiling point		N/A	Test substance is a solid.
830.7300	Density	496178-16	Y	1.3856 g/cm^3
830.7370	Dissociation constants in water	496178-19	Y	pK value not determined due to the absence of acidic or basic properties in water.
830.7550	Partition coefficient	496178-20	Y	Log P_{ow} = 5.46 at 20°C
830.7840	Water solubility:	496178-21	Y	57 µg/L @ 20°C
830.7950	Vapor pressure	496178-22	Y	2.0 x 10^{-5} hPa @ 25°C

Y = Acceptable; N = unacceptable (see Deficiency); N/A = Not Applicable; G = Data gap; I = In progress or need upgrade; U = Up-grade (additional information required

Enforcement Analytical Method: (MRID No. 496178-06)

This method is applicable for the determination of transfluthrin in TGAI or PAI. The technique consists of chiral-HPLC and detection by UV absorption. Quantification is carried out by comparing the peak areas observed for the compound in the sample with the peak areas of a reference solution of known content (external standard method). The method was validated for precision, accuracy, specificity and linearity.

3 Equipment and operating conditions

HPLC-Chromatograph:	e.g. Agilent HP1100 Series or any other suitable System
Pre-Colum:	Phenomenex Security Guard with 4 x 3 mm cartridge
Column:	250 x 4.6 mm, stainless steel
Stationary phase:	Phenomenex LUX Cellulose-1; 3 µm
Column temperature:	25°C
Mobile phase:	n-hexane / isopropanol = 97 / 3 (v/v)
Wavelength:	230 nm
Flow rate	1.0 mL / min
Injection volume	2 µl
Run time:	13 min (report time 10 min)

Remarks:

a) The column is expensive and may be easily damaged. Read manufacturers guide carefully before use. The HPLC column should be continuously rinsed with a minimum flow of 0.1 mL/min with the mobile phase. The column may be altered, if the temperature was changed.

b) In case of a worsening of the separation of species fresh isopropanol should be used. The retention times are most sensitive to slight changes in the isopropanol content.

CONFIDENTIAL APPENDIX

Manufacturing process information may be entitled to confidential treatment

830.1600 Description of Materials Used to Produce the Product: (MRID No. 496178-03)

[redacted]

830.1620. Description of Production Process: (MRID No. 496178-03)

[redacted]

CONFIDENTIAL APPENDIX:

830.1620 Description of the Production Process: (MRID No. 496178-03) con't.

[redacted]

CONFIDENTIAL APPENDIX:

830.1670. Discussion of the Formation of Impurities: (MRID No. 496178-04)

[redacted]

CONFIDENTIAL APPENDIX:

830.1670. Discussion of the Formation of Impurities: (MRID No. 496178-04) con't.

[redacted]

830.1700. Preliminary Analysis: (MRID No. 496178-05)

The enantiomeric purity of Transfluthrin was established by a chiral-HPLC/UV method. See the following page for the results of the preliminary analysis.

CONFIDENTIAL APPENDIX:

Results of the 5 batch analysis are provided in the following table:

[redacted]

Manufacturing process information may be entitled to confidential treatment